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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/918,637	08/01/2001	Ahmed Jehanli	01246.0134	2644

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EXAMINER	
HINES, JANA A	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 07/22/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/918,637	JEHANLI ET AL.	
	Examiner	Art Unit	
	Ja-Na Hines	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9,12,14-16 and 19-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,12,14-16 and 19-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on April 28, 2005 has been entered.

Amendment Entry

2. The amendment filed April 28, 2005 has been entered. Claims 1-3, 6, 8, 15-16 and 19, 21-23 have been amended. Claims 10-11, 13 and 17-18 have been cancelled. Claims 1-9, 12, 14-16, and 19-23 are under consideration in the office action.

Withdrawal of Rejections

3. The following rejections have been withdrawn in view of applicants' amendments and arguments:

a) The rejection of claim 3 is rejected under 35 U.S.C. 112, second paragraph;

b) The rejection of claims 1-3, 5-7, 9-10,12, 14-16 and 19-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jehanli et al., (1996) and Cole et al., (US Patent 4,589,612);

c) The rejection of claim 4 under 35 U.S.C. 103(a) as being unpatentable over Jehanli et al., (1996), and Cole et al., (US Patent 4,589,612) as applied to claim 1 above, and further in view of de Jaeger et al., (US Patent 4,837,168); and

d) The rejection of claim 8 under 35 U.S.C. 103(a) as being unpatentable over Jehanli et al., and Cole et al., further in view of Baker et al.

New Grounds of Rejection

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1-4,6,7, 9, 12, 14-15 are rejected under 35 U.S.C. 102(b) as being anticipated by de Jaeger et al., (US Patent 4,837,168 published June 6, 1989). The claims are drawn to a medical kit comprising a first part consisting of a dipstick coated with a drug conjugate and a second part which contains a labeled antidrug antibody being the specific binding partner of the drug conjugate and is adapted for receiving biological fluid, wherein the antibody is labeled with latex particles. The dependant claims are drawn to specific drugs, reagents, and materials for the first and second parts.

de Jaeger et al., teach a method of qualitatively or quantitatively determining a component of a complex formed between at least one specific binding protein and its

corresponding bindable substance (col. 2, lines 20-25). de Jaeger et al., teach the visualization of immunocomplexes using gold colloidal metal particles wherein specific techniques are referred to as sol particle immunoassays (col. 1, lines 54-65). The color signal is easily detected and optionally quantified either directly or if necessary after development (col. 2, lines 40-43). The optical properties of latex particles especially their color characteristics make them optimal labels (col. 2, lines 50-56). Examples of colored or colorable latex particles are well known in the art (col. 3-5, lines 10-40). de Jaeger et al., teach labeling one component of the complex with colored latex particles (col. 2, lines 27-39). de Jaeger et al., teach the immobilization of the bindable substance using well known techniques (col. 12, lines 6-10). The bindable substance to be detected is immobilized on an appropriate immobilizing solid support prior to its complexing with the labeled binding proteins, which are specific to the bindable substance (col.11-12, lines 67-5). In many cases, the specific binding proteins will be antibodies to specific antigens or haptens (col. 13, lines 15-17). The bindable substances which can be detected includes peptides, hormones, vitamins, polysaccharides, pharmacological agents and any other molecules for a specific binding counterpart exists in biological systems or that can be synthesized (col. 13, lines 58-64). Hapten analytes include the general class of drugs, hormones, vitamins, antimicrobial drugs and antibiotic drugs, steroids such as cortisol which is a corticosteroid, cardiac glycoside drugs, and a wide variety of other drugs (col. 14-15, lines 22-56). Thereby teach that any drug including a wide variety of antimicrobials and psycho-pharmaceutical agents are encompassed by de Jaeger et al. The immobilizing supports

can be made of a variety of polymeric materials or nitrocellulose and may take any convenient form such as sheets, welled plates, dip-sticks or the like (col. 12, lines 12-20). Thereby teaching a drug conjugate coated stick made of the same instantly claimed surface material. Example 1 teaches the preparation of latex bound antibodies (col. 17, lines 60-19). Example 2 teaches the design of a dipstick test in undiluted human serum (col. 19-21, lines 33-15). The immobilization procedures recite that bovine serum albumin was used to conjugate the drug and coat it onto the dipstick paper (col. 20, lines 27-39). The performance of the test recites that the dipstick was immersed into a mixture containing antibody coupled to colored latex beads, thus a container which could hold a dipstick held the labeled antibody solution thereby meeting the limitations of the claims (col. 20, lines 55-68).

It is noted that a recitation of the intended use, i.e., the qualitative or quantitative determination ability of the claimed kit must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. See *In re Casey*, 370 F.2d 576, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 312 F.2d 937, 939, 136 USPQ 458, 459 (CCPA 1963). In this case, the determination and time do not result in structural differences, thus de Jaeger et al., meets the limitations of the claims.

Thus, de Jaeger et al., teach a kit comprising a first part consisting of a dipstick coated with a drug conjugated to a bovine serum albumin protein and a tube shared container second part which contains colored latex particle labeled anti-drug antibody

being the specific binding partner of the drug conjugate and is adapted for receiving biological fluid, just as instantly claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 1-3, 5-7, 9,12, 14-16 and 19-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jehanli et al., (1996) and Cole et al., (US Patent 4,589,612) in view of Maggio (1987). The claims are drawn to a medical kit comprising a first part consisting of a dipstick coated with a drug conjugate and a second part which contains a labeled antidrug antibody being the specific binding partner of the drug conjugate and is adapted for receiving biological fluid, wherein the antibody is labeled with latex particles. The dependant claims are drawn to specific drugs, reagents, and materials for the first and second parts.

Jehanli et al., (1996) teach determination of Captopril, an orally active angiotension-converting enzyme drug, in human blood by an ELISA assay. The quantitation of captopril in biological fluids has been carried out previously in the art, however the author describes the development of a sensitive, simple and rapid ELISA assay for the determination of captopril (page 914). Preparation of rabbit serum albumin (RSA)-captopril conjugate for the immunoassay was disclosed again teaches a

drug conjugate (page 915). Thus making a drug conjugate as described by the claims to be between a drug and a protein. The microtitre strips were coated with the RSA-captopril (page 915). Anti-captopril antibody was added to the tube shaped wells and strips (page 915); thereby teaching a second part that contains labeled antibody and is adapted for receiving biological fluid. The strips were incubated for one hour at ambient temperatures and the washed bound antibody was revealed (page 915). Color development was terminated after 30 minutes (page 915). Human plasma samples containing various concentrations of the drug were tested and amounts of captopril were qualitatively or quantitatively determined (page 915). Jehanli et al., teach a medical kit and methods for qualitative or quantitative determination of a drug in a biological fluid comprising a first stick shaped part coated with a drug conjugate and a second tube-shaped part that contains a labeled antibody and is adapted for receiving biological fluid such as plasma wherein the first and second parts are contacted to indicate by color change the drug activity or presence. However Jehanli et al., do not teach antibodies labeled with gold material.

Cole et al., (US Patent 4,589,612) teach immunoassays can utilize a labeled component comprising a metal containing particle of a particular size and character to facilitate the maintenance of a generally stable, monodispersed suspension of the labeled component that was mixed and brought into contact with the sample to be analyzed (col. 4-5 lines 60-5). The labeled component can be an antibody labeled with metal particles such as gold sol particles which have been known in the art since 1975. Gold particles coated with antibody are intensely colored orange, red or violet

depending on particle size (col. 6-7 lines 60-2). The gold labeled antibodies can be directly visualized with the naked eye (col. 7 lines 8-11). Metal sol assays require fewer steps and fewer reagents and are considered more stable than most enzyme labeled antibodies (col. 7 lines 13-16). Moreover, such immunoassays can be used to detect controlled substances and other such small molecules (col. 9 lines 1-3). However neither Jehanli et al., nor Cole et al., teach the using a stick as the first part instead of a well.

Maggio teaches that in virtually all immunoassays either the antigen or antibody can be immobilized onto a solid phase (page 186). The solid phase carrier can be preformed into discs, tubes, sticks, microplates or the like (page 186). The advantage of the such preformed solid phases is that washing can be easily carried out by immersion of the tube, (stick), plates, etc., in the wash solution whereby in contrast other solid phase materials necessitate centrifugation which can be inconvenient (page 186). Polypropylene and polystyrene are well known materials which can form these solid phase carriers (page 187).

Therefore, it would have been prima facie obvious to modify the medical kit for qualitative or quantitative determination of a drug in a biological fluid comprising a first part coated with a drug conjugate and a second part that contains a labeled antibody and is adapted for receiving said fluid as taught by Jehanli et al., wherein no more than routine skill would have been required to incorporate the gold labeled antibody of Cole et al., and use a stick instead of a well as the solid phase carrier as taught by Maggio et al. One would have a reasonable expectation of success by incorporating an antibody

labeled with gold material, into the device and method of Jehanli et al., who already teach using the labeled antibodies to qualitatively or quantitatively determine the presence of a drug in a biological fluid. One skilled in the art would also have a reasonable expectation of success in replacing the solid phase well with a stick, since it offers the advantage of reducing the labor and offers easy and convenient wash steps. Moreover, no more than routine skill would have been required to use an alternative yet functionally equivalent labeled antibody in the medical kit and method of determination as taught by Jehanli et al., since only the expected results would have been obtained. A skilled artisan would have had a reasonable expectation of success in switching the antibody labels when the prior art teaches that metal sols require fewer steps and reagents and are considered more stable than most enzyme labeled antibodies. Likewise, no more than routine skill would have been required to use a stick instead of well, when either solid phase formation is known to be useful in the detection of analyte and be associated with time saving techniques.

6. Claims 8 and 22-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over de Jaeger et al., (US Patent 4,837,168) and Jehanli et al., (1996) as applied to claims 1-2 and 6-7 above, further in view of Baker et al., (US Patent 5,624,806 published April 1997). The de Jaeger et al., and Jehanli et al., references have been discussed above however neither teaches using Lisinopril as a drug conjugate or its associated antibodies.

Baker et al., teach antibodies to cardiac hypertrophy factors and their uses. Baker et al., teach that ACE inhibitors are angiotension-converting enzyme inhibiting drugs which prevent the conversion of angiotension I to angiotension II (col. 15 lines 47-50). ACE inhibitors that both prevent the conversion of angiotension I to angiotension II include the peptide drugs known as such as captopril and lisprinopril (col. 15 lines 55-57). Thus Baker et al., teach the antigen linsinopril along with antibodies to lisinopril.

It would have been prima facie obvious to modify the medical kit for qualitative or quantitative determination of a drug in a biological fluid comprising a first part coated with a drug conjugate and a second part that contains a labeled antibody and is adapted for receiving said fluid as taught by de Jaeger et al., and Jehanli et al., wherein no more than routine skill would have been required to incorporate the lisinopril drug conjugate an of Baker et al. One would have a reasonable expectation of success by incorporating the ACE drug lisinopril, when the prior art already teaches the determination of another ACE related drug which has similar functions into the kit and method of de Jaeger et al., and Jehanli et al., which already teach using the labeled antibodies to qualitatively or quantitatively determine the presence of a drug in a biological fluid. Moreover, no more than routine skill would have been required to use an alternative yet functionally equivalent drug and labeled antibody in the medical kit and method of determination as taught by de Jaeger et al., and Jehanli et al., since only the expected results would have been obtained. Baker et al., clearly teach that antibodies for the drugs are known in the art. Thus the use of alternative and functionally equivalent techniques would have been desirable to those of ordinary skill in the art based on the need to determine the

presence of the drug and the availability of drugs, drug conjugates and associated antibodies. A skilled artisan would have had a reasonable expectation of success in switching the ACE inhibitor drugs where the prior art already using one ACE drug can be detected and similar drugs are readily available.

Response to Arguments

7. Applicant's arguments filed April 28, 2005 have been fully considered. The examiner notes that the rejection of claims 1-3, 5-7, 9-10,12, 14-16 and 19-23 under 35 U.S.C. 103(a) as being unpatentable over Jehanli et al., (1996) and Cole et al., (US Patent 4,589,612) has been withdrawn. However, because two of the same references have been used in the new 35 U.S.C. 103(a) rejection applicants' arguments will be addressed below.

Applicants' assert that one would not have been motivated to combine the teachings of Jehanli et al., with those of Cole et al. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992).

In this case, Cole et al., teach the advantageous use of particles as labeling agents over the previous use of enzyme labels, as taught by Jehanli et al. Cole et al., clearly state many advantages of metal sol assays over enzyme labeled assays include: the require fewer steps; the use of fewer reagents; metal sols are considered more stable than most enzyme labels; the direct visualization of a result; and metal sols can detect controlled substances and other such small molecules.

Applicants' assertions that because antibody labeled gold particles are not taught by Jehanli et al., one skilled in the art would not have been motivated to exchange enzyme labels for gold particle labels , however those arguments are not persuasive for the reasons listed above. Moreover, no more than routine skill would have been required to use an alternative yet functionally equivalent labeled in the kit as taught by Jehanli et al., and Cole et al., since only the expected results would have been obtained when exchanging enzymes for particles; thus the use of alternative and functionally equivalent labeling agents would have been desirable to those of ordinary skill in the art based on the known advantageous.

Applicants' assert that the example of Cole et al., only disclose a competitive assay mode instead of sandwich mode. The MPEP section 2123 teaches that patents are relevant as prior art for all they contain, "The use of patents as references is not limited to what the patentees describe as their own inventions or to the problems with which they are concerned. They are part of the literature of the art, relevant for all they contain." *In re Heck*, 699 F.2d 1331, 1332-33, 216 USPQ 1038, 1039 (Fed. Cir. 1983) (quoting *In re Lemelson*, 397 F.2d 1006, 1009, 158 USPQ 275, 277 (CCPA 1968)). A

reference may be relied upon for all that it would have reasonably suggested to one having ordinary skill the art, including nonpreferred embodiments. *Merck & Co. v. Biocraft Laboratories*, 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989). See also *Celeritas Technologies Ltd. v. Rockwell International Corp.*, 150 F.3d 1354, 1361, 47 USPQ2d 1516, 1522-23 (Fed. Cir.1998) (The court held that the prior art anticipated the claims even though it taught away from the claimed invention. "The fact that a modem with a single carrier data signal is shown to be less than optimal does not vitiate the fact that it is disclosed."). Therefore applicants' argument is not persuasive especially when considering the advantages taught by Cole et al. and Maggio.

Applicant's arguments with respect to the claim now requiring a stick have been considered however those arguments are moot in view of the new grounds of rejection. The art teaches the solid phase microtitre strips and wells as disclosed by Jehanli et al., and Cole et al., are easily interchangeable with other solid phase carriers. Moreover, Maggio teaches advantages in using solid phases that can be washed out easily by immersion of the tube, stick, or plate. Therefore, contrary to applicants' assertions about the lack of obviousness, Maggio clearly provides motivation for why one skilled in the art would be motivated to use a stick instead of a well even though both of those carriers are equivalent.

Applicants argue that Jehanli et al., do not teach qualitative or quantitative determination of a drug is achieved within at least 5 minutes but less than 30 minutes of the first part contacting the second part. However applicant is reminded that the claims

are drawn to a kit. Thus a recitation of the intended use, such as determination of the drug with 5 to 30 minutes, must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. There is no structural difference between the conjugate drug and label antibody of the prior art and those instantly claimed. Therefore the components described by Jehanli et al., Cole et al., and Maggio teach the instantly claimed kit, including a stick. Since the prior art structures are capable of performing the intended use, they meet the claimed requirements.

Conclusion

8. No Claims allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is 571-272-0859. The examiner can normally be reached on Monday-Thursday and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on 571-272-0864. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Ja-Na Hines
June 29, 2005